

**REMARKS**

New claims 31-43 are submitted, hereby, in place of claims 15-30. The instant Amendment limits the scope of the claims to formulae actually corresponding to the compounds described in the application. The  $\Delta$  group is the only group which definition has not been amended, since  $\Delta$  refers to functional groups, which are decisive regarding the immunogenicity of the claimed compounds.

The definition of the  $\theta$  group has been modified so as to exclude sequences having an alanine in the fourth position. Thus, all sequences have a leucine in said position. These compounds have superior properties, as compared to peptides having an alanine in the fourth position (see discussion, below, regarding Charneau et al.).

**35 USC § 112, second paragraph:**

Concerning the claims relating to the diagnostic kit, the limitation "for the detection of HIV-1 group O specific antibodies" has been added, according to the Examiner's suggestion. Applicants submit that there is a need to further specify the steps involved both in the immunoassay method claims and the diagnostic kit claims according to the presently claimed invention. Indeed the invention, the designed peptidic sequences and their use for detection purposes can be based on any immunoassay method well known by those skilled in the art. There is no reason why the structure of these peptides should restrict the detection method to a specific embodiment. In any event, examples 2, 3 and 4 of the specification constitute embodiments with

precise guidelines allowing those skilled in the art to make and sue the invention.

**35 USC 102 (novelty):**

The peptide LNLWGCRGKAICYTSVQWNETWG disclosed in Charneau et al (1996) does not met the limitation of claim 31. Indeed the peptide sequence between the two conserved motif WGC and CYTS corresponds to group  $\Theta$  of formula I. The RGKAI sequence, as depicted in Charneau et al, is not one of the sequences SEQ ID n° 15-20, expressly described for the  $\Theta$  group in claim 31. Indeed, the inventors specifically excluded peptides having an alanine residue in fourth position since they revealed that the presence of a leucine instead of an alanine in this position improves the detection sensitivity in immunoassays (see comparative tests and results reported in the attached Appendix). Therefore the subject matter of the present claims is novel over Charneau et al.

**35 USC 103 (non-obviousness):**

The background of the invention:

The technical background of the present application is the development of synthetic peptides for the detection of infections due to group O HIV-1 virus.

It is known to diagnose HIV infections by detecting antibodies against an immunodominant region of protein gp 41. Such diagnostic tests often rely on natural peptide sequences derived from isolates. This strategy turned out to fail for the detection of some group O HIV-1 infected patients. Indeed, this immunodominant epitope in gp 41 proved to be greatly divergent among group O HIV-1 viruses. Therefore it appeared very difficult to guarantee the serological screening

of individuals by means of antigens from one and the same isolate.

The invention:

Owing to the huge variability of HIV-1 group O isolates, the inventors developed artificial peptide sequences different from the peptides encoded by known viral strains. Among the developed peptides, those which displayed a bettered sensitivity as compared to the prior art peptides can be represented by the general formula:  $\Delta$  - Z - WGC -  $\theta$  - CYTS -  $\Omega$ . Therefore the present invention allows the development of highly sensitive diagnostic tests of group O HIV-1 infections based on the use of a single synthetic peptide.

Brust et al (1998) discloses the peptide MVP 601-623 of sequence NQQRNLNWGCKGKLICYTSVKWN, which is directly derived from the HIV-1 group O isolate MVP 5180/91.

The statement of rejection alleges that this peptide contains the same main motif WGC- $\theta$ -CYTS as recited in the present claims and, particularly, the same sequence KGKLI. Yet the MVP 601-623 sequence does not meet the limitations of claim 31. Moreover, as emphasized in the statement of rejection, this sequence is the critical epitope of the designed peptides.

Peptide MVP 601-623 cannot reasonably be expected to display the same antigenic and immunologic properties as the presently claimed invention. Actually, the instant specification demonstrates the opposite. The present application describes a MVP 5180 peptide which is 35 residue long and comprises the MVP 601-623 sequence. In example 3, a comparative immunoenzymatic test is carried out with peptides of the invention and prior art peptides derived

from natural isolates, one of which is MVP 5180. Table VI of the specification summarizes the detection sensitivities observed with the different peptides. The results are figured by letters A to D, corresponding to different levels of sensitivity, from limit of detection (A) to high sensitivity (D). Table VI clearly illustrates the superior immunoreactivity of peptides according to the invention (for instance peptides of SEQ ID n° 14-16) as compared to the MVP 5180 peptide.

Thus, it was not *prima facie* obvious to design artificial peptides comprising a modified major epitope, as compared to sequences derived from natural HIV-1 group O strains (as disclosed in Brust et al), while allowing an bettered performance for the detection of HIV-1 group O infections.

Furthermore, this result is unexpected because the the presently claimed invention provides for detection of all known strains of HIV-1 group O viruses using a single artificial peptide, better than provided for by the natural peptides previously derived from viral strains.

**35 USC 112, first paragraph:**

Claims have been amended to narrow the scope of the claims. In particular, the range of the possibilities for the  $\Theta$  group, which is the major epitope of the peptides has been strictly limited to the sequences expressly described and displaying the desired immunogenicity.

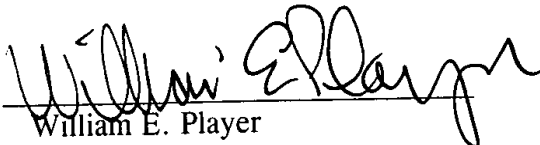
The definition of group Z, as well as the  $\Omega$  group definition, have been simplified and consequently cover a reduced number of sequences.

U.S. Patent Application No.: 09/147,362  
Attorney Docket No.: P63163US0

Favorable action is requested..

Respectfully submitted,

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Date: July 30, 2001

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